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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/476,290	12/30/1999	EUGENE M JOHNSON	6029-2669	7622
21888	7590	03/23/2004	EXAMINER	
THOMPSON COBURN, LLP ONE US BANK PLAZA SUITE 3500 ST LOUIS, MO 63101			PAK, MICHAEL D	
			ART UNIT	PAPER NUMBER
			1646	

DATE MAILED: 03/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/476,290	Applicant(s) JOHNSON ET AL.	
	Examiner Michael Pak	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 October 2003.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 99-126 is/are pending in the application.
4a) Of the above claim(s) 107-126 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 99-106 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>4-6-00</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of III in Paper filed 24 October 2003 is acknowledged.

Claims 107-126 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 99-106 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 99 recite the term "capable of reacting" which is ambiguous because the metes and bounds of the term is clear. One skilled in the art usually uses the term "bind" when describing antibody binding to the antigen. The term "react" has the chemical meaning of undergoing a chemical change. However, the claims are drawn to an antibody binding to antigen as supported by the specification and the term "capable

of reacting" describes a chemical change of the products involved which is confusing.

Claims 100-106 are dependent on claim 99 and encompass the term.

Claim 106 recites the limitation "oligonucleotide" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 106 recite the term "oligonucleotide" which is confusing because generally nucleotides do not comprise an amino acid sequence.

3. Claim 106 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 106 recite the term "oligonucleotide" which is new matter because the specification does not disclose a nucleotide which comprise an amino acid sequence.

4. Claim 99-106 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 99-106 encompass an antibody which reacts with a large genus of variants and fragments of growth factor because of recitation of "65% identity" without a

functional limitation of the polypeptide. However, the specification discloses the specific species of SEQ ID NO: of neurturin polypeptides. The disclosure is not provided for the genus of variants without functional limitation. The *University of California v. Eli Lilly and Co. (CAFC) 43 USPQ2d 1398* held that a generic claim to human or mammalian when only the rat protein sequence was disclosed did not have written description in the specification. Thus, the genus of neurturin with a specific structure cannot be envisioned.

5. Claims 99-106 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated or purified antibodies which bind neurturin polypeptide with at least 65% identity to the claimed SEQ ID NO: and a specific function of neurturin, does not reasonably provide the full scope of enablement for antibodies claimed without functional claim limitations. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims encompass an antibody which binds a neurturin variant which is 65% identical with no functional limitation of the neurturin variant. Claims encompass active domain of neurturin which are non-functional as well as domains with functions which has not been disclosed in the specification. However, the specification does not teach how to make and use active domain of neurturin or growth factors which are non-functional as well as domains with functions which has not been disclosed in the specification. It would require undue experimentation to use active domains of neurturin

because the specification does not provide guidance to determine the active domains of all growth factors. Callard et al.(V) disclose that there are at least six different kind of structural families of cytokines which are a subgenus of growth factors based on X-ray and NMR studies(see Callard et al., page 3, second paragraph and Table1.1). Thus, the activation domain of one family of cytokine such as "cysteine knot" family is different structurally from any other family member such as "chemokines" (Callard et al.(V), Pages 4-5, Fig.1.1). Furthermore, Kingsley (AP; Genes and Dev., 1994)) teach that additional mutagenesis, binding, and structural studies are required to identify the portions of the molecule responsible for interacting with receptors (page 134, sentence bridging left and right column). It would require undue experimentation to use active domains of neurturin or other growth factors because the specification does not provide guidance to determine the active domains of neurturin or other growth factors. The additional mutagenesis, binding, and structural studies required to identify the portions of the molecule responsible for different functions would require empirical and undue experimentation. The specification does not provide guidance to determine the X-ray or NMR studies to determine the structure of active domains of neurturin or other growth factors. Growth factors encompass large number of subgenus which are grouped according to structural or functional similarity and one subgenus has very little if any similarity with another subgenus of growth factors. For example, neurturin is only 40% related to the closest neurotrophic factor, glial derived neurotrophic factor, and the three dimensional structure of neither proteins are known. The proper protein conformation of the protein for a functional interaction with other proteins such as receptors are sensitive

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to perturbation in the changes in the primary amino acid sequence. Bowie et al. (Science, 1990) teach the unpredictability in the structure art because the prediction of structure from sequence is an extremely complex art and it is unlikely that the problem will be solved in an exact manner in the near future (page 1307, column 1). Furthermore, substitutions are unpredictable because some positions do not tolerate any substitutions (page 1307, column 2).

Without such guidance the experimentation necessary to make and use antibody which bind variant neurturin or growth factor is undue. In view of the extent and the unpredictability of the experimentation required to practice the invention as claimed, one skilled in the art could not make the invention without undue experimentation.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

6. Claims 99-106 are rejected under 35 U.S.C. 102(e) as being anticipated by Lin et al.. (US 6,362,319) with evidence of Harlow et al. (Antibodies, 1988).

Lin et al. teach the antibodies that recognize GDNF (columns 5 and 44-46). The SEQ ID NO:33-41 are fragments of oligopeptide which is identical to the fragments of GDNF amino acid sequence. Since antibodies recognize smaller portion of the whole protein and GDNF has sequences which overlap with Neurtuin the antibodies of Lin et al. would bind a neurturin polypeptide with at least 65% identity to SEQ ID NO:1, 2, 7 and 8. Harlow et al. teach that only 6 amino acid epitope is needed to generate an antibody (Harlow et al., page 76).

7. No claims allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Pak whose telephone number is 571-272-0879. The examiner can normally be reached on 8:30 am - 2:00 pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 571-272-0871. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9306 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-0507.

Michael D. Pak

Michael Pak
Primary Examiner
Art Unit 1646
March 8, 2004